| WHAT | IS | CLA | IMED | IS: |
|------|----|-----|------|-----|
|------|----|-----|------|-----|

| _ | _ | | |
|----|---|--------------|-------------|
| 1 | 7 | dompocition | COMPTICIPA |
| Ι. | _ | composition, | comprising: |

| 5 | Fori | a nula | huma | an ir | nterl | leuk: | in-3 | muta | ant p | poly | pept: | ide (| of tl | ne | |
|----|----------|-----------|-------|-------|------------|-------|------|------|-------|------------|-------|-------|-------|-----|-------------------|
| | Ala 1 | Pro | Met | Thr | Gln 5 | Thr | Thr | Ser | Leu | Lys 10 | Thr | Ser | Trp | Val | Asr 15 |
| 10 | Cys | Xaa | Xaa | Xaa | Xaa 20 | | Xaa | Xaa | Xaa | Xaa 25 | Xaa | Xaa | Xaa | Xaa | Ха <i>а</i> 30 |
| 15 | Xaa | Xaa | Xaa | Xaa | Xaa 35 | | Xaa | Xaa | Asn | Xaa 40 | Xaa | Xaa | Xaa | Xaa | Xaa |
| LJ | Xaa | Xaa | Xaa | Xaa | Xaa 50 | | Xaa | Xaa | Xaa | Xaa 55 | Xaa | Xaa | Xaa | Xaa | Xaa |
| 20 | Xaa | Xaa | Xaa | Xaa | Xaa 65 | | Xaa | Xaa | Xaa | Xaa 70 | Xaa | Xaa | Xaa | Xaa | Xaa 75 |
| | Xaa | Xaa | Xaa | Xaa | Xaa 80 | | Xaa | Xaa | Xaa | Xaa 85 | Xaa | Xaa | Xaa | Xaa | Xaa 90 |
| 25 | Xaa | Xaa | Xaa | Xaa | Xaa 95 | | Xaa | Xaa | Xaa | Xaa 100 | Xaa | Xaa | Xaa | | Xaa 105 |
| | Xaa | Phe | Xaa | Xaa | Xaa 110 | | Xaa | Xaa | Xaa | Xaa 115 | Xaa | Xaa | Xaa | | Xaa 120 |
| 30 | | | Xaa | | Gln 125 | | Thr | Leu | Ser | Leu 130 | Ala | Ile | Phe | | |
| | [SEÇ | O ID | NO: 1 | L] | | | | | | | | | | | |

35 wherein

Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or

Arg;

- Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
- Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
 - Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
- Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, Gln, Leu, Val or Gly;
 - Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
 Phe, Leu, Ser, or Arg;
 - Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or
- 15 Leu;
 - Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala:
 - Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
- 20 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
 Trp;
 - Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
 - Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,
- 25 Leu, or Lys;
 - Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or
 Gln;
 - Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
 or Glu;
- 30 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;
 - Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
 Thr, Arg, Ala, Phe, Ile or Met;
 - Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;
- 35 Xaa at position 36 is Asp, Leu, or Val;
 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;

- Xaa at position 38 is Asn, or Ala;
- Xaa at position 40 is Leu, Trp, or Arg;
- Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro;
- 5 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala;

 - Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro;
 - Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;
- 15 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His;
 - Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;
 - Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val, His, Phe, Met or Gln;
 - Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- 25 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
 - Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or Met;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
 30 Asn, Lys, His, Ala or Leu;
 - Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
 - Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,
 His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
 - Xaa at position 57 is Asn or Gly;
- 35 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

- Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or
 - aa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser:
- 5 Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, Asp, or Ile;
 - Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro,
 or Val;
 - Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;
 - Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
 Pro, or His;
 - Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;
- 20 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
 - Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn;
 - Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg,
 or Asp;
- 25 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;
 - Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
 - Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;
- 30 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
 - Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
 - Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- 35 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or Asp;

- Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or Arg;
- Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
 or Lys;
- 5 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
 - Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
 - Xaa at position 85 is Leu, Asn, Val, or Gln;
- 10 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
 - Xaa at position 87 is Leu, Ser, Trp, or Gly;
 - Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
 - Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, or Ser;
- 15 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or Met;
 - Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His;
 - Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, Ile or Leu;
 - Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;
 - Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, His, Ala, or Pro;
- 25 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
 - Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
 - Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
 - Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
- 30 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
 Gly, Ser, Phe, or His;
- Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;

- Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- Xaa at position 103 is Asp, or Ser;
- Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
- 5 Leu, Gln, Lys, Ala, Phe, or Gly;
 - Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
 Tyr, Leu, Lys, Ile, Asp, or His;
 - Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;
- 10 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, Ser, Ala or Pro;
 - Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
 or Gly;
- Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln,
 His, Glu, Ser, Ala, or Trp;
 - Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;
 - Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;
 - Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile, Val or Asn;
 - Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;
- 25 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile;
 - Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;
- 30 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr:
- Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or 35 Gln;
 - Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,

25

or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15

10 amino acids can be deleted from the C-terminus; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133) human interleukin-3;

- a colony stimulating factor; and at least one non-toxic pharmaceutically acceptable carrier.
 - 2. A composition, comprising:
- 20 a human interleukin-3 mutant polypeptide of the Formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
1 5 10 15

Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Leu Lys Xaa Xaa 20 25 30

Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu Xaa 50 55 60

35 Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile Glu 65 70 75

Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr Ala 80 85 90 5 Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa Xaa 95 100 105 Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Leu Glu Xaa 115 120 110 10 Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe [SEQ ID NO:2] 125 130 wherein 15 Xaa at position 17 is Ser, Gly, Asp, Met, or Gln; Xaa at position 18 is Asn, His, or Ile; Xaa at position 19 is Met or Ile; Xaa at position 21 is Asp or Glu; Xaa at position 23 is Ile, Ala, Leu, or Gly; 20 Xaa at position 24 is Ile, Val, or Leu; Xaa at position 25 is Thr, His, Gln, or Ala; Xaa at position 26 is His or Ala; Xaa at position 29 is Gln, Asn, or Val; Xaa at position 30 is Pro, Gly, or Gln; 25 Xaa at position 31 is Pro, Asp, Gly, or Gln; Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu; Xaa at position 33 is Pro or Glu; Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg, 30 Gln, Glu, Ile, Phe, Thr or Met; Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val; Xaa at position 37 is Phe, Ser, Pro, or Trp; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Asp, Ser, Cys, Ala, Asn, Ile, 35 Leu, Met, Tyr or Arg; Xaa at position 44 is Asp or Glu;

Xaa at position 45 is Gln, Val, Met, Leu, Thr, Ala, Asn, Glu, Ser or Lys;

Xaa at position 46 is Asp, Phe, Ser, Thr, Ala, Asn Gln,
 Glu, His, Ile, Lys, Tyr, Val or Cys;

5 Xaa at position 50 is Glu, Ala, Asn, Ser or Asp;
Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;

Xaa at position 54 is Arg or Ala;

Xaa at position 55 is Arg, Thr, Val, Leu, or Gly;

Xaa at position 56 is Pro, Gly, Ser, Gln, Ala, Arg, Asn, Glu, Leu, Thr, Val or Lys;

Xaa at position 60 is Ala or Ser;

Xaa at position 62 is Asn, Pro, Thr, or Ile;

Xaa at position 63 is Arg or Lys;

15 Xaa at position 64 is Ala or Asn;

Xaa at position 65 is Val or Thr;

Xaa at position 66 is Lys or Arg;

Xaa at position 67 is Ser, Phe, or His;

Xaa at position 68 is Leu, Ile, Phe, or His;

20 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or Gly;

Xaa at position 71 is Ala, Pro, or Arg;

Xaa at position 72 is Ser, Glu, Arg, or Asp;

Xaa at position 73 is Ala or Leu;

Xaa at position 76 is Ser, Val, Ala, Asn, Glu, Pro, or Gly;

Xaa at position 77 is Ile or Leu;

Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Arg, Ile, Gly, or Asp;

30 Xaa at position 80 is Asn, Gly, Glu, or Arg;

Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
 Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;

Xaa at position 83 is Pro or Thr;

Xaa at position 85 is Leu or Val;

35 Xaa at position 87 is Leu or Ser;

Xaa at position 88 is Ala or Trp;

Xaa at position 91 is Ala or Pro;

Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg;

Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn,

5 Phe, Ser or Thr;

Xaa at position 96 is Pro or Tyr;

Xaa at position 97 is Ile or Val;

Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Leu, Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;

10 Xaa at position 99 is Ile, Leu, or Val;

Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Pro, Asn, Ile, Leu or Tyr;

Xaa at position 104 is Trp or Leu;

Xaa at position 105 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His;

Xaa at position 106 is Glu or Gly;

Xaa at position 108 is Arg, Ala, or Ser;

Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;

20 Xaa at position 112 is Thr, Val, or Gln;

Xaa at position 114 is Tyr or Trp;

Xaa at position 115 is Leu or Ala;

25 Xaa at position 117 is Thr or Ser;

Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;

Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,

30 His, Ile, Tyr, or Cys;

and which can additionally have Met- preceding the amino

35 acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15

amino acids can be deleted from the C-terminus; and wherein from 4 to 35 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133) human interleukin-3;

a colony stimulating factor selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF); and

at least one non-toxic pharmaceutically acceptable carrier.

15

3. A composition of claim 2, wherein said human interleukin-3 mutant polypeptide is of the Formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn

20 1 5 10 15

Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa 20 25 30

25 Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa 35 40 45

Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala
50 55 60

30

35

Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu
65 70 75

Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala

Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Gly Asp Trp Xaa 95 100 105 Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa 5 110 115 120 Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe 125 130 [SEQ ID NO:3] 10 wherein Xaa at position 17 is Ser, Gly, Asp, or Gln; Xaa at position 18 is Asn, His, or Ile; Xaa at position 23 is Ile, Ala, Leu, or Gly; 15 Xaa at position 25 is Thr, His, or Gln; Xaa at position 26 is His or Ala; Xaa at position 29 is Gln or Asn; Xaa at position 30 is Pro or Gly; Xaa at position 32 is Leu, Arg, Asn, or Ala; 20 Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met; Xaa at position 35 is Leu, Ala, Asn, or Pro; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Asp, Ser, Ala, Asn, Ile, Leu, 25 Met, Tyr or Arg; Xaa at position 45 is Gln, Val, Met, Leu, Ala, Asn, Glu, or Lys; Xaa at position 46 is Asp, Phe, Ser, Gln, Glu, His, Val or Thr; 30 Xaa at position 50 is Glu Asn, Ser or Asp; Xaa at position 51 is Asn, Arg, Pro, Thr, or His; Xaa at position 55 is Arg, Leu, or Gly; Xaa at position 56 is Pro, Gly, Ser, Ala, Asn, Val, Leu or Gln; 35 Xaa at position 62 is Asn, Pro, or Thr; Xaa at position 64 is Ala or Asn;

217

```
Xaa at position 65 is Val or Thr;
     Xaa at position 67 is Ser or Phe;
     Xaa at position 68 is Leu or Phe;
     Xaa at position 69 is Gln, Ala, Glu, or Arg;
     Xaa at position 76 is Ser, Val, Asn, Pro, or Gly;
 5
     Xaa at position 77 is Ile or Leu;
     Xaa at position 79 is Lys, Gly, Asn, Met, Arg, Ile, or
           Gly;
     Xaa at position 80 is Asn, Gly, Glu, or Arg;
10
     Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
           His, Met, Phe, Ser, Thr, Tyr or Val;
     Xaa at position 87 is Leu or Ser;
     Xaa at position 88 is Ala or Trp;
     Xaa at position 91 is Ala or Pro;
     Xaa at position 93 is Thr, Asp, or Ala;
15
     Xaa at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser or
           Thr:
     Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu,
           Lys, Met, Ser, Tyr, Val or Leu;
20
     Xaa at position 99 is Ile or Leu;
     Xaa at position 100 is Lys or Arg;
     Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Pro,
           Asn, Ile, Leu or Tyr;
     Xaa at position 105 is Asn, Pro, Ser, Ile or Asp;
25
     Xaa at position 108 is Arg, Ala, or Ser;
     Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
     Xaa at position 112 is Thr or Gln;
     Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, Tyr
           or Ile;
30
     Xaa at position 117 is Thr or Ser;
     Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
     Xaa at position 121 is Ala, Ser, Ile, Pro, or Asp;
     Xaa at position 122 is Gln, Met, Trp, Phe, Pro, His, Ile,
           or Tyr;
```

Xaa at position 123 is Ala, Met, Glu, Ser, or Leu;

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and wherein

- 5 from 4 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133)human interleukin-3.
- 4. A composition of claim 3, wherein said human 10 interleukin-3 mutant polypeptide is of the Formula:

Xaa at position 42 is Gly, Asp, Ser, Ile, Leu, Met, Tyr, or Ala;

Xaa at position 45 is Gln, Val, Met or Asn;

15 Xaa at position 46 is Asp, Ser, Gln, His or Val;

Xaa at position 50 is Glu or Asp;

Xaa at position 51 is Asn, Pro or Thr;

Xaa at position 62 is Asn or Pro;

Xaa at position 76 is Ser, or Pro;

20 Xaa at position 82 is Leu, Trp, Asp, Asn Glu, His, Phe, Ser or Tyr;

Xaa at position 95 is His, Arg, Thr, Asn or Ser;

25 Xaa at position 100 is Lys or Arg;

Xaa at position 101 is Asp, Pro, His, Asn, Ile or Leu;

Xaa at position 105 is Asn, or Pro;

Xaa at position 108 is Arg, Ala, or Ser;

Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, or

a human interleukin-3 mutant polypeptide of the

30 Tyr;

Xaa at position 121 is Ala, or Ile;

Xaa at position 122 is Gln, or Ile; and

Xaa at position 123 is Ala, Met or Glu.

35
5. A composition, comprising:

Formula:

| 5 | Asn 1 | Cys | Xaa | Xaa | Xaa 5 | Xaa | Xaa | Xaa | Xaa | Хаа 10 | Xaa | Xaa | Xaa | Xaa | Хаа 15 |
|----|----------|------|----------------|-----|------------|-----|-------|-------|------|------------|-----|-------|-------|-------|------------|
| 5 | Xaa | Xaa | Xaa | Xaa | Xaa 20 | Xaa | Xaa | Xaa | Xaa | Asn 25 | Xaa | Xaa | Xaa | Xaa | Xaa 30 |
| 10 | Xaa | Xaa | Xaa | Xaa | Xaa 35 | Xaa | Xaa | Xaa | Xaa | Xaa 40 | Xaa | Xaa | Xaa | Xaa | Xaa 45 |
| | Xaa | Xaa | Xaa | Xaa | Xaa 50 | Xaa | Xaa | Xaa | Xaa | Xaa 55 | Xaa | Xaa | Xaa | Xaa | Xaa 60 |
| 15 | Xaa | Xaa | Xaa | Xaa | Xaa 65 | Xaa | Xaa | Xaa | Xaa | Xaa 70 | Xaa | Xaa | Xaa | Xaa | Xaa 75 |
| | Xaa | Xaa | Xaa | Xaa | Xaa 80 | Xaa | Xaa | Xaa | Xaa | Xaa 85 | Xaa | Xaa | Xaa | Xaa | Xaa 90 |
| 20 | Xaa | Xaa | Phe | Xaa | Xaa 95 | Xaa | Xaa | Xaa | Xaa | Xaa 100 | Xaa | Xaa | Xaa | Xaa | Xaa 105 |
| 25 | Xaa | Xaa | Xaa | Xaa | Gln 110 | Gln | [SEÇ |) ID | NO:4 | 1] | | | | | |
| | wher | cein | | | | | | | | | | | | | |
| | Xaa | at p | posit | ion | 3 is | Ser | ., Ly | /s, (| Sly, | Asp, | Met | ;, G] | ln, d | or Ai | g; |
| | Xaa | at p | posit | ion | 4 is | Asr | ı, Hi | is, I | Leu, | Ile, | Phe | e, Ar | g, d | or Gl | ln; |
| 30 | | | posit | | | | | | | | | | | | |
| | | | osit | | | | | | | | | | | | la; |
| | Xaa | | posit | | | | | | | Arg, | Ala | ı, Gl | Ly, C | Slu, | |
| | Xaa | | ln, A posit | | | | | | | Ser. | Ala | ı. Hi | s. A | Asp. | |
| 35 | | | sn, G | | | | | | | , | | -, | , • | -~ | |
| | Xaa | | osit | | | | | _ | | Leu, | Gly | , Tr | p, I | ys, | |

15

Phe, Leu, Ser, or Arg;

- Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;
- Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or Ala:
 - Xaa at position 12 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
 - Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala;
 - Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
- 10 Trp;
 - Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val;
 - Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys;
 - Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or

 - Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu;
 - Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
- 20 Thr, Arg, Ala, Phe, Ile or Met;
 - Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or Val:
 - Xaa at position 22 is Asp, Leu, or Val;
 - Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile;
- 25 Xaa at position 24 is Asn, or Ala;
 - Xaa at position 26 is Leu, Trp, or Arg;
 - Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro;
 - Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn,
 Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met;
- 30 Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly or Ser;

 - Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr,
- 35 Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp;
 Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,

- Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
- Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or His;
- Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;

- 10 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His:
 - Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,

 Ser, Met, or;
 - Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
 Asn, Lys, His, Ala or Leu;
 - Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly;
 - Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,
- His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
 - Xaa at position 43 is Asn or Gly;
 - Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
 - Xaa at position 45 is Glu Tyr, His, Leu, Pro, or Arg;
- 25 Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr;
 - Xaa at position 47 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
 - Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;
- 30 Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;
 - Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys;
 - Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- 35 Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;

- Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;
- 5 Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;
 - Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;
- Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;

 - Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 15 Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;

 - Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu;
- 20 Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg:

 - Xaa at position 66 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
 or Arg;

 - Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- 30 Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;
 - Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;
 - Xaa at position 71 is Leu, Asn, Val, or Gln;
 - Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;
 - Xaa at position 73 is Leu, Ser, Trp, or Gly;
- Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;
 Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His,

Asn, or Ser;

- Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
 or Met;
- Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
 or His;
- Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, Ile or Leu;
- Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;
- 10 Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, His, Ala or Pro;
 - Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;
 - Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 15 Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;
 - Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr, Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- 20 Xaa at position 86 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, Pro;
 - Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val, Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;
 - Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or
- 25 Pro;
 - Xaa at position 89 is Asp, or Ser;
 - Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
 Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;
 - Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, Ser, Ala, or Pro;
- 35 Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;

- Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg,
 His, Glu, Ser, Ala or Trp;
- Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;
- Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser,
- 5 or Phe;
 - Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
 Asp, Lys, Leu, Ile, Val or Asn;
 - Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;
- Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met;
 - Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile;
- 15 Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;
 - Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
 or Tyr;
 - Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
 or Arg;
 - Xaa at position 106 is Asn, Ala, Pro, Leu, His, Val, or Gln:
 - Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
 or Gly;
- Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys;
 - Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;
- and which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding native amino acids of (1-133) human interleukin-3;
- a colony stimulating factor selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently

| referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), |
|--|
| IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL- |
| 11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B- |
| cell growth factor, B-cell differentiation factor, |
| eosinophil differentiation factor and stem cell factor |
| (SCF); and |

at least one non-toxic pharmaceutically acceptable carrier.

10 6. A composition of claim 5, wherein said human interleukin-3 mutant polypeptide is of the Formula:

Asn Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Leu Lys Xaa 1 5 10 15

15

Xaa Xaa Xaa Xaa Xaa Asp Xaa Asn Leu Asn Xaa Glu Xaa 20 25 30

Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Asn Leu Glu 20 35 40 45

Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Ile
50 55 60

25 Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr 65 70 75

Ala Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa 80 85 90

30

Xaa Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu 95 100 105

35 Xaa Xaa Xaa Gln Gln [SEQ ID NO:5]

wherein

Xaa at position 3 is Ser, Gly, Asp, Met, or Gln;

Xaa at position 4 is Asn, His, or Ile;

5 Xaa at position 5 is Met or Ile;

Xaa at position 7 is Asp or Glu;

Xaa at position 9 is Ile, Ala, Leu, or Gly;

Xaa at position 10 is Ile, Val, or Leu;

Xaa at position 11 is Thr, His, Gln, or Ala;

10 Xaa at position 12 is His or Ala;

Xaa at position 15 is Gln, Asn, or Val;

Xaa at position 16 is Pro, Gly, or Gln;

Xaa at position 17 is Pro, Asp, Gly, or Gln;

Xaa at position 18 is Leu, Arg, Gln, Asn, Gly, Ala, or

15 Glu;

Xaa at position 19 is Pro or Glu;

Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Ala, Arg, Gln, Glu, Ile, Phe, Thr or Met;

Xaa at position 21 is Leu, Ala, Asn, Pro, Gln, or Val;

20 Xaa at position 23 is Phe, Ser, Pro, or Trp;

Xaa at position 24 is Asn or Ala;

Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Asn, Ile, Leu, Met Tyr or Arg;

Xaa at position 30 is Asp or Glu;

25 Xaa at position 31 is Gln, Val, Met, Leu, Thr, Ala, Asn, Glu, Ser or Lys;

Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln,
 Glu, His, Ile, Lys, Tyr, Val or Cys;

Xaa at position 36 is Glu, Ala, Asn, Ser or Asp;

30 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His;

Xaa at position 40 is Arg or Ala;

Xaa at position 41 is Arg, Thr, Val, Leu, or Gly;

Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,

35 Glu, Leu, Thr, Val or Lys;

Xaa at position 46 is Ala or Ser;

```
Xaa at position 48 is Asn, Pro, Thr, or Ile;
     Xaa at position 49 is Arg or Lys;
     Xaa at position 50 is Ala or Asn;
     Xaa at position 51 is Val or Thr;
 5
     Xaa at position 52 is Lys or Arg;
     Xaa at position 53 is Ser, Phe, or His;
     Xaa at position 54 is Leu, Ile, Phe, or His;
     Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, or
           Gly;
10
     Xaa at position 57 is Ala, Pro, or Arg;
     Xaa at position 58 is Ser, Glu, Arg, or Asp;
     Xaa at position 59 is Ala or Leu;
     Xaa at position 62 is Ser, Val, Ala, Asn, Glu, Pro, or
           Gly;
15
     Xaa at position 63 is Ile or Leu;
     Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
           Gly, or Asp;
     Xaa at position 66 is Asn, Gly, Glu, or Arg;
     Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
20
           Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
     Xaa at position 69 is Pro or Thr;
     Xaa at position 71 is Leu or Val;
     Xaa at position 73 is Leu or Ser;
     Xaa at position 74 is Ala or Trp;
25
     Xaa at position 77 is Ala or Pro;
     Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or
           Arg;
     Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn,
           Phe, Ser or Thr;
30
     Xaa at position 82 is Pro or Tyr;
     Xaa at position 83 is Ile or Val;
     Xaa at position 84 is His, Ile, Asn, Leu, Ala, Thr, Leu,
           Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
     Xaa at position 85 is Ile, Leu, or Val;
35
     Xaa at position 86 is Lys, Arg, Ile, Gln, Pro, or Ser;
     Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Asn,
```

Ile, Leu or Tyr;

Xaa at position 90 is Trp or Leu;

Xaa at position 91 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, Asp, or His;

5 Xaa at position 92 is Glu, or Gly;

Xaa at position 94 is Arg, Ala, or Ser;

Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;

Xaa at position 98 is Thr, Val, or Gln;

Xaa at position 100 is Tyr or Trp;

10 Xaa at position 101 is Leu or Ala;

Xaa at position 103 is Thr or Ser;

Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;

15 Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly;

Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 35 of the amino acids designated by Xaa are different from the

- 25 corresponding amino acids of native human interleukin-3.
 - 7. A composition of claim 6, wherein said human interleukin-3 mutant polypeptide is of the Formula:
- 30 Asn Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa 1 5 10 15

Xaa Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp
20 25 30

35

20

Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu

| | | | | 35 | | | | | 40 | | | | | 45 |
|----|-------------------------|----------------------------------|-------------------------|----------------------|----------------------|--------------------------------|--------------------|------------------|-------------|------|-------|------|------|------------|
| _ | Ala P | he Xa | a Arg | Xaa 50 | Xaa | Lys | Xaa | Xaa | Xaa 55 | Asn | Ala | Ser | Ala | Ile 60 |
| 5 | Glu X | aa Xa | a Leu | Xaa 65 | Xaa | Leu | Xaa | Pro | Cys 70 | Leu | Pro | Xaa | Xaa | Thr 75 |
| 10 | Ala X | aa Pr | o Xaa | Arg 80 | Xaa | Pro | Ile | Xaa | Xaa 85 | Xaa | Xaa | Gly | Asp | Trp 90 |
| | Xaa G | lu Ph | e Xaa | Xaa 95 | Lys | Leu | Xaa | Phe | Tyr 100 | Leu | Xaa | Xaa | | Glu 105 |
| 15 | Xaa X | aa Xa | a Xaa | Gln 110 | Gln | [SEÇ | Q ID | NO:6 | 5] | | | | | |
| | where | in | | | | | | | | | | | | |
| 20 | Xaa a Xaa a | t pos t pos t pos t pos | ition ition | 4 is | Ası | n, Hi | is, d | or Il .eu, | .e; or G | | | | | |
| 25 | Xaa a Xaa a Xaa a | t pos t pos t pos t pos t pos | ition ition ition | 15 i 16 i 18 i | s Gl s Pi s Le | ln or co or eu, <i>P</i> | Asr Gly Arg, | n; '; Asn, | | | | Sln, | Glu, | |
| 30 | Xaa a | Ile, t pos t pos t pos | ition | 21 i 24 i | s Le | eu, A sn or | : Ala | ι; | | | | Ile, | Leu, | |
| | Xaa a | t pos | Tyr o | | _ | .n, V | /al, | Met, | Leu | , Al | .a, A | Asn, | Glu | or |
| 35 | Xaa a | Lys; t pos: Val | ition or The | | s As | sp, F | he, | Ser, | Ala | , Gl | .n, G | Slu, | His, | |

```
Xaa at position 36 is Glu, Asn, Ser or Asp;
     Xaa at position 37 is Asn, Arg, Pro, Thr, or His;
     Xaa at position 41 is Arg, Leu, or Gly;
     Xaa at position 42 is Pro, Gly, Ser, Ala, Asn, Val, Leu or
 5
     Xaa at position 48 is Asn, Pro, or Thr;
     Xaa at position 50 is Ala or Asn;
     Xaa at position 51 is Val or Thr;
     Xaa at position 53 is Ser or Phe;
10
     Xaa at position 54 is Leu or Phe;
     Xaa at position 55 is Gln, Ala, Glu, or Arg;
     Xaa at position 62 is Ser, Val, Asn, Pro, or Gly;
     Xaa at position 63 is Ile or Leu;
     Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly;
15
     Xaa at position 66 is Asn, Gly, Glu, or Arg;
     Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
           His, Met, Phe, Ser, Thr, Tyr or Val;
     Xaa at position 73 is Leu or Ser;
     Xaa at position 74 is Ala or Trp;
20
     Xaa at position 77 is Ala or Pro;
     Xaa at position 79 is Thr, Asp, or Ala;
     Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser or
           Thr;
     Xaa at position 84 is His, Ile, Asn, Ala, Thr, Arg, Gln,
25
           Glu, Lys, Met, Ser, Tyr, Val or Leu;
     Xaa at position 85 is Ile or Leu;
     Xaa at position 86 is Lys or Arg;
     Xaa at position 87 is Asp, Pro, Met, Lys, His, Pro, Asn,
           Ile, Leu or Tyr;
30
     Xaa at position 91 is Asn, Pro, Ser, Ile or Asp;
     Xaa at position 94 is Arg, Ala, or Ser;
     Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
     Xaa at position 98 is Thr or Gln;
     Xaa at position 102 is Lys, Val, Trp, or Ile;
35
     Xaa at position 103 is Thr, Ala, His, Phe, Tyr or Ser;
     Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
```

Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp;
Xaa at position 108 is Gln, Met, Trp, Phe, Pro, His, Ile,
 or Tyr;

Xaa at position 109 is Ala, Met, Glu, Ser, or Leu;

5

and which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 26 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133)human

- 10 interleukin-3.
 - 8. The composition of claim 7, wherein said human interleukin-3 mutant polypeptide is of the Formula:

15

Xaa at position 17 is Ser, Lys, Asp, Met, Gln, or Arg; Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;

Xaa at position 19 is Met, Arg, Gly, Ala, or Cys;

- 20 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
 - Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, or Val;
- Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, or Gly;
 - Xaa at position 23 is Ile, Ala, Gly, Trp, Lys, Leu, Ser,
 or Arg;

Xaa at position 24 is Ile, Gly, Arg, or Ser;

Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or

30 Ala:

Xaa at position 26 is His, Thr, Phe, Gly, Ala, or Trp;

Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;

Xaa at position 28 is Lys, Leu, Gln, Gly, Pro, Val or Trp;

Xaa at position 29 is Gln, Asn, Pro, Arg, or Val;

35 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys;

- Xaa at position 31 is Pro, Asp, Gly, Arg, Leu, or Gln;
- Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu:
- Xaa at position 33 is Pro, Leu, Gln, Thr, or Glu;
- 5 Xaa at position 34 is Leu, Gly, Ser, or Lys;
 - Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, or Gln;
 - Xaa at position 36 is Asp, Leu, or Val;
 - Xaa at position 37 is Phe, Ser, or Pro;
 - Xaa at position 38 is Asn, or Ala;
- 10 Xaa at position 40 is Leu, Trp, or Arg;
 - Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, Pro;
 - Xaa at position 42 is Gly, Asp, Ser, Cys, or Ala;
 - Xaa at position 42 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, or Ser;
- 15 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, or Pro;
 - Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, or Trp;
 - Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, or Gly;
- 20 Xaa at position 47 is Ile, Gly, Ser, Arg, Pro, or His;
 - Xaa at position 48 is Leu, Ser, Cys, Arg, His, Phe, or Asn;
 - Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
 or Asp;
- 25 Xaa at position 50 is Glu, Leu, Thr, Asp, or Tyr;
 - Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
 His;
 - Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- 30 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser. or:
 - Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
 or Leu;
 - Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- 35 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, or Lys; Xaa at position 57 is Asn or Gly;



Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;

Xaa at position 60 is Ala, Ser, Tyr, Asn, or Thr;

5 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser:

Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, or Ile;

Xaa at position 63 is Arg, Tyr, Trp, Ser, Pro, or Val;

Xaa at position 64 is Ala, Asn, Ser, or Lys;

Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;

Xaa at position 66 is Lys, Ile, Val, Asn, Glu, or Ser;

15 Xaa at position 68 is Leu, Val, Trp, Ser, Thr, or His;

Xaa at position 69 is Gln, Ala, Pro, Thr, Arg, Trp, Gly,
 or Leu;

Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;

Xaa at position 71 is Ala, Met, Leu, Arg, Glu, Thr, Gln,

Trp, or Asn;

Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg,
 or Asp;

Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;

25 Xaa at position 74 is Ile, Thr, Pro, Arg, Gly, Ala;

Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;

30 Xaa at position 77 is Ile, Ser, Arg, or Thr;

Xaa at position 78 is Leu, Ala, Ser, Glu, Gly, or Arg;

Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Ile, or Asp;

Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, or

35 Arg;

Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, or



Lys;

Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, or Asp;

Xaa at position 83 is Pro, Thr, Trp, Arg, or Met;

Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;

5 Xaa at position 85 is Leu, Asn, or Gln;

Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 87 is Leu, Ser, Trp, or Gly;

Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,

10 or Asn;

Xaa at position 90 is Ala, Ser, Asp, Ile, or Met;

Xaa at position 91 is Ala, Ser, Thr, Phe, Leu, Asp, or His;

Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, or

15 Leu;

Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;

Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, or Pro;

20 Xaa at position 95 is His, Gln, Pro, Val, Leu, Thr or Tyr;

Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

Xaa at position 97 is Ile, Lys, Ala, or Asn;

Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, or Pro;

25 Xaa at position 99 is Ile, Arg, Asp, Pro, Gln, Gly, Phe, or His;

Xaa at position 100 is Lys, Tyr, Leu, His, Ile, Ser, Gln,
 or Pro;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,

30 Tyr, or Gln;

Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro:

Xaa at position 103 is Asp, or Ser;

Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,

35 Leu, Gln, Lys, Ala, Phe, or Gly;

Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,

| | Ty: | r, Leu, | Lys | , I | le, o | r His | ; | | | | |
|-----|------|---------|-----|-----|-------|-------|------|------|------|------|-----|
| Xaa | at p | osition | 106 | is | Glu, | Ser, | Ala, | Lys, | Thr, | Ile, | Gly |
| | or | | | | | | | | | | |

- Xaa at position 108 is Arg, Asp, Leu, Thr, Ile, or Pro;
 5 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly.
 - 9. A composition of claim 8, wherein said human interleukin-3 mutant polypeptide is of the Formula:

\$1\$ \$5\$ \$10\$ (Met) $_m\text{-Ala}$ Pro Met Thr Gln Thr Thr Ser Leu Lys Thr

15 20

Ser Trp Val Asn Cys Ser Xaa Xaa Xaa Asp Glu Ile Ile

15 25 30 35

Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa
40 45 50

Xaa Asn Leu Asn Xaa Glu Asp Xaa Asp Ile Leu Xaa Glu 55 60

- 20 Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa 65 70 75
 - Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa 80 85

Ile Leu Xaa Asn Leu Xaa Pro Cys Xaa Pro Xaa Xaa Thr

25 90 95 100

Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly
105 110 115

Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu 120 125

30 Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln Thr Thr Leu 130

Ser Leu Ala Ile Phe [SEQ ID NO:7]

wherein m is 0 or 1; Xaa at position 18 is Asn or Ile; Xaa at position 19 is Met, Ala or Ile; Xaa at position 20 is Ile, Pro or Ile; Xaa at position 23 is Ile, Ala or Leu; Xaa

at position 25 is Thr or His; Xaa at position 29 is Gln, Arg, Val or Ile; Xaa at position 32 is Leu, Ala, Asn or Arg; Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe, Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa 5 at position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at position 45 is Gln, Val, or Met; Xaa at position 46 is Asp or Ser; Xaa at position 49 is Met, Ile, Leu or Asp; Xaa at position 50 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at position 55 is Arg, Leu, or Thr; Xaa at 10 position 56 is Pro or Ser; Xaa at position 59 is Glu or Leu; Xaa at position 60 is Ala or Ser; Xaa at position 62 is Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, His or Gln; Xaa at position 69 is Gln or Glu; Xaa at 15 position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at position 79 is Lys, Arg or Ser; Xaa at position 82 is Leu, Glu, Val or Trp; Xaa at position 85 is Leu or Val; Xaa at position 87 is Leu, Ser, Tyr; Xaa at position 88 is Ala or Trp; Xaa at position 91 is Ala or 20 Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or Thr; Xaa at position 98 is His, Ile, or Thr; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at position 105 is Asn or Glu; Xaa at position 109 is Arg, Glu or Leu; Xaa at position 112 is Thr 25 or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; Xaa at position 117 is Thr or Ser; Xaa at position 120 is Asn, Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding 30 amino acids of native human interleukin-3.

10. The composition of claim 9, wherein said human interleukin-3 mutant polypeptide is of the Formula:

35 1 5 10 (Metm-Alan)p-Asn Cys Ser Xaa Xaa Xaa Asp Glu Xaa Ile

15 20

Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa

25 30 35

Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa Ile Leu Xaa Glu

238

40 45

Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa 50 55 60

Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa 65 70 75

Ile Leu Xaa Asn Xaa Xaa Pro Cys Xaa Pro Xaa Ala Thr

Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Kaa Gly
90 95 100

10 Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu

Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln [SEQ ID NO:8]

wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at 15 position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile: Xaa at position 6 is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xaa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Ile; Xaa at position 18 is Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; 20 Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile or Asp; Xaa at position 36 is Glu or Asp; Xaa at position 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or 25 Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala or Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is Val or Ser; Xaa at position 30 53 is Ser, Asn, His or Gln; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or Trp; Xaa at position 71 is Leu or Val; 35 Xaa at position 73 is Leu, Ser or Tyr; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at

position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87 is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95 is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His; Xaa at position 109 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125) human interleukin-3.

11. The composition of claim 10, wherein said human interleukin-3 mutant polypeptide is of the Formula:

15

20

10

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:9];

25 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
30 Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:10];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35 Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser

Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Pro Asn

240

Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:11];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:12];

15

20

10

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:13];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
30 Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:14];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu

35 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Pro Asn

241

Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:15];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:16];

15

20

10

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:17];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
30 Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:18];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu

35 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn

242

Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:19];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:20];

15

20

10

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:21];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
30 Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:22];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35 Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn

243

Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:23];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:24];

15

20

10

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:25];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:26];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu

35 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Pro Asn

244

Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:27];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

10 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:28];

15

20

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:29];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:30];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

245

Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:31];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn

10 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:32];

15

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:33];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:34];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35 Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser

Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:35];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:36];

15

20

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:37];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:38];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala

Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

15

25

35

247

Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:39].

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp

10 Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Asp Arg
Asn Leu Arg Leu Ser Asn Leu Glu Ser Phe Val Arg Ala Val Lys
Asn Leu Glu Asn Ala Ser

Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:40]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His Leu Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp 20 Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr

Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:41]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

10 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:42]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala

248

Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:43]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

10 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

15 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:44]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

20 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

25 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:45]

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro 30 Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Gln Gln Gln [SEQ ID NO:46] and

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:47].

12. The composition of claim 10, wherein said human interleukin-3 mutant polypeptide is of the Formula:

15

20

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His Leu Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Gln Ala Gln Glu Gln Gln [SEQ ID NO:48].

25

- 13. The composition of claim 1-12 wherein said CSF is selected from the group consisting of G-CSF, Meg-CSF and GM-CSF:
- 14. A method of increasing multi-lineage

 30 hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of a human interleukin-3 mutant polypeptide of the Formula:
- 35 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15

| \ | Cys | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
|-----|---|-------|-------|------|-------------|-------|-------|------|------|-----|-------|----------|------|------|-----------|
| | | | | | 20 | | | | | 25 | | | | | 30 |
| _ \ | _ | | | | | | | | _ | | | | | | |
| 5 | Xaa | Xaa | Xaa | Xaa | | | Xaa | Xaa | Asn | | Xaa | Xaa | Xaa | Xaa | |
| | \ | | | | 35 | | | | | 40 | | | | | 45 |
| | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | | | 50 | | | | | 55 | | | | | 60 |
| 10 | | | / | | | | | | | | | | | | |
| | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | | ` | \ 65 | | | | | 70 | | | | | 75 |
| | | | | | \ | ١ | | | | | | | | | |
| 15 | хаа | хаа | хаа | xaa | хаа 80 | | хаа | хаа | Xaa | 85 | хаа | хаа | хаа | хаа | хаа 90 |
| 10 | | | | | Ų Ū | \ | | 4 | | 03 | | | | | 50 |
| | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | *aa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | | | 95 | | () | X | | 100 | | | | | 105 |
| | | | | | | | | | | | | | | | |
| 20 | Xaa | Phe | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | | | | 110 | | | | | 115 | | | | | 120 |
| | Vaa | Vaa | Vaa | Gln | Gln | Thr. | Thr | Leu | Ser | 1.2 | ב 1 מ | Tla | Dhe | | |
| | naa | naa | Add | GIII | 125 | 1111 | 1111 | Dea | 261 | 130 | \ | 116 | FILE | | |
| 25 | [SEÇ |) IDI | NO:15 | 5] | | | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| | wher | ein | | | | | | | | | | | | | |
| | Xaa | at p | posit | ion | 17 i | s Se | er, I | Ĺys, | Gly, | Asp | , Me | et, ò | Jn, | or | |
| 2.0 | Arg; | | | | | | | | | | | | | | |
| 30 | <pre>Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, Gln;</pre> | | | | | | | | | | Arg, | \range r | | | |
| | Хаа | | | ion | 19 i | .s Me | et, I | ?he, | Ile, | Arc | r, G1 | .v. I | Ala, | or | \ |
| | | | ys; | | | | | • | | _ | | 1, | • | | |
| | Xaa | at p | posit | ion | 20 i | s Il | le, C | Cys, | Gln, | Glu | ı, Ar | g, E | Pro, | or | \ |
| 35 | | A. | la; | | | | | | | | | | | | |
| | Xaa | at p | posit | ion | 21 i | s As | sp, I | Phe, | Lys, | Arg | r, Al | .a, G | Sly, | Glu, | |

Gln, Asn, Thr, Ser or Val; Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, Gln, Leu, Val or Gly; Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys, 5 Phe, Leu, Ser, or Arg; Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu: Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala; 10 Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala; Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or Trp; Xaa at position 29 is Gla Asn, Leu, Pro, Arg, or Val; 15 Xaa at position 30 is Fro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys; Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 20 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; Xaa at position 34 is Leu, Val, Gly, Sex, Lys, Glu, Gln, Thr, Arg, Ala, Phe, Ile or Met; 25 Xaa at position 35 is Leu, Ala, Gly, Asn, Pko, Gln, or Val; Xaa at position 36 is Asp, Leu, or Val; Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; Xaa at position 38 is Asn, or Ala; 30 Xaa at position 40 is Leu, Trp, or Arg; Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro: Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala; 35 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly or Ser;

```
Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
           Trp, Glu, Asn, Gln, Ala or Pro;
     Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
           Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;
 5
     Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,
           Òln, Lys, His, Ala, Tyr, Ile, Val or Gly;
     Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or
           His;
     Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe,
10
           Glu, Lys, Thr, Ala, Met, Val or Asn;
     Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
           or Asp;
     Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,
           Ser, Ala, Ile, Val, His, Phe, Met or Gln;
15
     Xaa at position 51 is Asp, Arg, Met, Pro, Ser, Thr, or
           His;
     Xaa at position 52 is Asn,
                                Ais, Arg, Leu, Gly, Ser, or
           Thr;
     Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,
20
           Ser, or Met;
     Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
           Asn, Lys, His, Ala or Leu;
     Xaa at position 55 is Arg, Thr, Val, Ser\ Leu, or Gly;
     Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,
25
           His, Thr, Ala, Tyr, Phe, Leu, Val or Mys;
     Xaa at position 57 is Asn or Gly;
     Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or
           Cys;
     Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
30
     Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;
     Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, ox
           Ser;
     Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, Asp,
           Ile;
35
     Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro,
           or Val;
```

Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or 5 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His; Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His; Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, 10 Gly, or Lau; Xaa at position 7 is Asn, Leu, Val, Trp, Pro, or Ala; Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn's 15 Xaa at position 72 is Sex, Glu, Met, Ala, His, Asn, Arg, or Asp; Xaa at position 73 is/Ala, GAu, Asp, Leu, Ser, Gly, Thr, or Arg; Xaa at position 74 is IIe, Met, Thr, Pro, Arg, Gly, Ala; 20 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu; Xaa at position 76 is Ser, Val, Ala, Ash, Trp, Glu, Pro, Gly, or Asp; Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu; 25 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile or Asp; Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, 30 or Arg; Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or Lys; Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; 35 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met; Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;

```
Xaa at position 85 is Leu, Asn, Val, or Gln;
     Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
     Xaa at position 87 is Leu, Ser, Trp, or Gly;
     Xaa\at position 88 is Ala, Lys, Arg, Val, or Trp;
 5
     Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
           Asn, or Ser;
     Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
           or Met;
     Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
10
           or His;
     Xaa at position 32 is Pro, Phe, Arg, Ser, Lys, His, Ala,
           Gly, Ile or Deu;
     Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
           or Arg;
     Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
15
           Lys, His, Ala, or Pro;
     Xaa at position 95 is His, Aln, Pro, Arg, Val, Leu, Gly,
           Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
     Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
20
     Xaa at position 97 is Ile, Val, Eys, Ala, or Asn;
     Xaa at position 98 is His, Ile, Ash, Leu, Asp, Ala, Thr,
           Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
     Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
           Gly, Ser, Phe, or His;
25
     Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
           Gln, or Pro;
     Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
           Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;
     Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
30
           Pro;
     Xaa at position 103 is Asp, or Ser;
     Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
           Leu, Gln, Lys, Ala, Phe, or Gly;
     Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
35
           Tyr, Leu, Lys, Ile, Asp, or His;
     Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
```

10

25

or Pro;

Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, Ser, Ala or Pro;

Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;

Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His, Glu, Ser, Ala, or Trp;

Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;

Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;

Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu Ile, Val or Asn;

Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;

15 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met;

Xaa at position 116 is Lys, Leu Pro, Thr, Met, Asp, Val, Glu, Arg, Trp, Ser, Asn His, Ala, Tyr, Phe, Gln, or Ile;

20 Xaa at position 117 is Thr. Ser, Asn, Ile, Trp, Lys, or Pro:

Xaa at position 118 is Leu, Ser, Pro Ala, Glu, Cys, Asp, or Tyr;

Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg;

Xaa at position 120 is Asn, Ala, Pro, Leu, Nis, Val, or Gln;

30 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys;

Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids

10

20

35

can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-183) human interleukin-3; and

a colony stimulating factor selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF).

15. A method of increasing multi-lineage hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of human interleukin-3 mutant polypeptide of the Formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
1 5 10 15

Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Leu Lys Xaa Xaa 25 20 25 30

Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa Xaa
35 40 45

30 Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu Xaa 50 55 60

Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Ile Glu

Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr Ala

80 85 90 Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa Xaa 95 100 105 5 Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Leu Glu Xaa 110 115 120 Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe 10 125 130 [SEQ ID NO: 3] wherein Xaa at position 1% is Ser, Gly, Asp, Met, or Gln; 15 Xaa at position 18 \(\s Asn, His, or Ile; \) Xaa at position 19 is Met or Ile; Xaa at position 21 is Asp or Glu; Xaa at position 23 is Ile Ala, Leu, or Gly; Xaa at position 24 is I/e, Val, or Leu; 20 Xaa at position 25 is Thr, HAs, Gln, or Ala; Xaa at position 26 is His of Ala; Xaa at position 29 is Glm, Asn, or Val; Xaa at position 30 is Pro, Gly, or Gln; Xaa at position 31 is Pro, Asp, Gly, or Gln; 25 Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu; Xaa at position 33 is Pro or Glu; Xaa at position 34 is Leu, Val, Gly, Ser, Lya, Ala, Arg, Gln, Glu, Ile, Phe, Thr or Met; 30 Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, ok Val; Xaa at position 37 is Phe, Ser, Pro, or Trp; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Asp, Ser, Cys, Ala, Asn, Ila Leu, Met, Tyr or Arg; 35 Xaa at position 44 is Asp or Glu; Xaa at position 45 is Gln, Val, Met, Leu, Thr, Ala, Asn,

```
Glu, Ser or Lys;
     Xaa at position 46 is Asp, Phe, Ser, Thr, Ala, Asn Gln,
           Glu, His, Ile, Lys, Tyr, Val or Cys;
     Xaa at position 50 is Glu, Ala, Asn, Ser or Asp;
 5
     Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
           His;
     Xaa at position 54 is Arg or Ala;
     Xaa at position 55 is Arg, Thr, Val, Leu, or Gly;
     Xaa at position 56 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
10
           Glu, Lau, Thr, Val or Lys;
     Xaa at position 60 is Ala or Ser;
     Xaa at position 62 is Asn, Pro, Thr, or Ile;
     Xaa at position 63 is Arg or Lys;
     Xaa at position 64 is Ala or Asn;
15
     Xaa at position 65 is Val or Thr;
     Xaa at position 66 is bys or Arg;
     Xaa at position 67 is Sex, Phe, or His;
     Xaa at position 68 is Leu, le, Phe, or His;
     Xaa at position 69 is/Gln,/Ala, Pro, Thr, Glu, Arg, or
20
           Gly;
     Xaa at position 71 is A/a, Pro, or Arg;
     Xaa at position 72 is Ser, Qu, Arg, or Asp;
     Xaa at position 73 is Ala or Let;
     Xaa at position 76 is Ser, Val, Ala, Asn, Glu, Pro, or
25
           Gly;
     Xaa at position 77 is Ile or Leu;
     Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
           Gly, or Asp;
     Xaa at position 80 is Asn, Gly, Glu, or Arg;
30
     Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
           Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
     Xaa at position 83 is Pro or Thr;
     Xaa at position 85 is Leu or Val;
     Xaa at position 87 is Leu or Ser;
35
     Xaa at position 88 is Ala or Trp;
     Xaa at position 91 is Ala or Pro;
```

Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg;

Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn, Phe, Ser or Thr;

5 Xaa at position 96 is Pro or Tyr;

Xaa at\position 97 is Ile or Val;

Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Leu, Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;

Xaa at position 99 is Ile, Leu, or Val;

10 Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser;
Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Pro,
Asn, Ile, Let or Tyr;

Xaa at position 104 is Trp or Leu;

Xaa at position 105 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,

15 Leu, Lys, Ile, Asp, or His;

Xaa at position 106 is Gly on Gly;

Xaa at position 108 is rg, Ala, or Ser;

Xaa at position 109 is/Arg / Thk, Glu, Leu, or Ser;

Xaa at position 112 is Thr, Val, or Gln;

20 Xaa at position 114 is Tyr or Trp;

Xaa at position 115 is Leu or Ala;

Xaa at position 116 is Lys, Thr, Val, Trp, Ser, Ala, His, Met, Phe, Tyr or Ile;

Xaa at position 117 is Thr or Ser;

Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Pho, Pro, His, Ile, Tyr, or Cys;

30 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15

amino acids can be deleted from the C-terminus; and wherein

| (| from 4 to 35 of the amino acids designated by Xaa are | | | | | | | | | | | | |
|--|---|-----|--|--|--|--|--|--|--|--|--|--|--|
| | different from the corresponding amino acids of native (1- | | | | | | | | | | | | |
| ` | 133) human interleukin-3; and | | | | | | | | | | | | |
| 5 | A pharmaceutically effective amount of a colony stimulating factor. | | | | | | | | | | | | |
| 16. The method of claim 15, wherein said human | | | | | | | | | | | | | |
| | interleukin-3 mutant polypeptide is of the Formula: | | | | | | | | | | | | |
| 10 | | | | | | | | | | | | | |
| | Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val | Asn | | | | | | | | | | | |
| | 1 5 10 | 15 | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa | Xaa | | | | | | | | | | | |
| 15 [°] | 20 25 | 30 | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | Pro Xaa Pro Xaa Xaa Asp\Phe Xaa Asn Leu Asn Xaa Glu Asp | Xaa | | | | | | | | | | | |
| | 35 40 | 45 | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| 20 | Xaa Ile Leu Met Xaa Xaa Asn Deu Arg Xaa Xaa Asn Leu Glu | Ala | | | | | | | | | | | |
| | 50 / 55 | 60 | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile | Glu | | | | | | | | | | | |
| | 65 | 75 | | | | | | | | | | | |
| 25 | | | | | | | | | | | | | |
| | Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr | Ala | | | | | | | | | | | |
| | 80 85 | 90 | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gay Asp Trp | Xaa | | | | | | | | | | | |
| 30 | | 105 | | | | | | | | | | | |
| | | | | | | | | | | | | | |
| | Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu | Xaa | | | | | | | | | | | |
| | 110 115 | 120 | | | | | | | | | | | |
| | 110 | | | | | | | | | | | | |
| 35 | Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe | | | | | | | | | | | | |
| | 125 130 | | | | | | | | | | | | |
| | [SEQ ID NO:3] | | | | | | | | | | | | |

```
wherein
     Xaa at position 17 is Ser, Gly, Asp, or Gln;
     Xaa at position 18 is Asn, His, or Ile;
     Xaa at position 23 is Ile, Ala, Leu, or Gly;
     Xaa at position 25 is Thr, His, or Gln;
     Xaa at position 26 is His or Ala;
     Xaa at position 29 is Gln or Asn;
     Xaa at\position 30 is Pro or Gly;
10
     Xaa at position 32 is Leu, Arg, Asn, or Ala;
     Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
           Ile, Pke, Thr, or Met;
     Xaa at position 35 is Leu, Ala, Asn, or Pro;
     Xaa at position 38 is Asn or Ala;
15
     Xaa at position 42\is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
           Met, Tyr or Arg
     Xaa at position 45 is 3n, Val, Met, Leu, Ala, Asn, Glu,
           or Lys;
                                 Phe, Ber, Gln, Glu, His, Val
     Xaa at position 46 is Asp,
20
           or Thr:
     Xaa at position 50 is Glu Asn, Ser or Asp;
     Xaa at position 51 is Asm, Arg, Pro, Thr, or His;
     Xaa at position 55 is Arg Leu, on Gly;
     Xaa at position 56 is Pro, Gly, Ser\ \alphala, Asn, Val, Leu or
25
           Gln;
     Xaa at position 62 is Asn, Pro, or Thr;
     Xaa at position 64 is Ala or Asn;
     Xaa at position 65 is Val or Thr;
     Xaa at position 67 is Ser or Phe;
30
     Xaa at position 68 is Leu or Phe;
     Xaa at position 69 is Gln, Ala, Glu, or Arg;
     Xaa at position 76 is Ser, Val, Asn, Pro, or Gly;
     Xaa at position 77 is Ile or Leu;
     Xaa at position 79 is Lys, Gly, Asn, Met, Arg, Ile, or
35
           Gly;
     Xaa at position 80 is Asn, Gly, Glu, or Arg;
```

Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser, Thr, Tyr or Val; Xaa at position 87 is Leu or Ser; Xaa at position 88 is Ala or Trp; 5 Xaa at position 91 is Ala or Pro; Xàa at position 93 is Thr, Asp, or Ala; Xaa\at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser or Thr: Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu, 10 Lys Met, Ser, Tyr, Val or Leu; Xaa at position 99 is Ile or Leu; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Pro, Asn, Ile, Leu or Tyr; 15 Xaa at position 105\is Asn, Pro, Ser, Ile or Asp; Xaa at position 108 is Arg, Ala, or Ser; Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser; Xaa at position 112 is The or Gln; Xaa at position 116 is Lys, Val, Tro, Ala, His, Phe, Tyr 20 or Ile: Xaa at position 117 is Thr or/Ser; Xaa at position 120 is Ash, Pro, Leu, His, Val, or Gln; Xaa at position 121 is Ala, Ser, Te, Pro, or Asp; Xaa at position 122 is Gln, Met, Txp\ Phe, Pro, His, Ile, 25 or Tyr; Xaa at position 123 is Ala, Met, Glu, Sex, or Leu; and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids 30 can be deleted from the N-terminus and/or from χ to 15 amino acids can be deleted from the C-terminus; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133) human interleukin-3: and 35 a colony stimulating factor selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently

referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor

17. The method of claim 16, wherein said human interleukin-3 mutant polypeptide is of the Formula:

10

5

NSCF).

Xaa at position 42 is Gly, Asp, Ser, Ile, Leu, Met, Tyr, or Ala;

Xaa at position 45 is Gln, Val, Met or Asn;

Xaa at position 46 is Asp, Ser, Gln, His or Val;

15 Xaa at position 30 is Glu or Asp;

Xaa at position 51 is Asn, Pro or Thr;

Xaa at position 62 is Asn or Pro;

Xaa at position 76 is Ser, or Pro;

Xaa at position 82 is/Let, Trp, Asp, Asn Glu, His, Phe,

20 Ser or Tyr;

Xaa at position 95 is His/ Arg, Thr, Asn or Ser;

Xaa at position 98 is His, Ile, Leu, Ala, Gln, Lys, Met,

Ser, Tyr or Val;

Xaa at position 100 is Lys or Arg

25 Xaa at position 101 is Asp, Pro, His, Asn, Ile or Leu;

Xaa at position 105 is Asn, or Pro;

Xaa at position 108 is Arg, Ala, or Sex;

Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, or Tyr;

30 Xaa at position 121 is Ala, or Ile;

Xaa at position 122 is Gln, or Ile; and

Xaa at position 123 is Ala, Met or Glu.

18. A method of increasing multi-lineage hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of a human interleukin-3 mutant

polypeptide of the Formula: Xaa\Xaa Xaa Xaa Xaa Xaa Xaa Xaa Aan Xaa <u>X</u>aa <u>X</u>aa Xaa Xaa Xaa Xaa Xaa Xaa 🗱 🖎 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gln Gln [SEQ IN NO: wherein Xaa at position 3 is Ser, Lys, Gly, Asp, Mat, Gln, or Arg; Xaa at position 4 is Asn, His, Leu, Ile, Phe Arg, or Gln; Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys; Xaa at position 6 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala; Xaa at position 7 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, Asn, Thr, Ser or Val; Xaa at position 8 is Glu, Trp, Pro, Ser, Ala, His, Asp Asn, Gln, Leu, Val, or Gly; Xaa at position 9 is Ile, Val, Ala, Leu, Gly, Trp, Lys,

Phe, Leu, Ser, or Arg; Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or Leu; Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or 5 Xaa at\position 12 is His, Thr, Phe, Gly, Arg, Ala, or Trk; Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala; Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or 10 Trp; Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val; Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys; Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or 15 Xaa at position 18 is Leu Val, Arg, Gln, Asn, Gly, Ala, or Glu; Xaa at position 19 is Pro, Lety Gln, Ala, Thr, or Glu; Xaa at position 20 is Leu/Val/ Gly, Ser, Lys, Glu, Gln, 20 Thr, Arg, Ala, Phe, Ile/or Met; Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or Val: Xaa at position 22 is Asp, Leu, or Val; Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile; 25 Xaa at position 24 is Asn, or Ala; Xaa at position 26 is Leu, Trp, or Arg; Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro; Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn, Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met; 30 Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly or Ser; Xaa at position 30 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro; Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr, 35 Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp; Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,

Gln, Lys, His, Ala, Tyr, Ile, Val or Gly; Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or His; Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe, 5 Glu, Lys, Thr, Ala, Met, Val or Asn; Xaa\at position 35 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp; Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Sex, Ala, Ile, Val, His, Phe, Met or Gln; Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or 10 His; Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr; Xaa at position 3% is Leu, Thr, Ala, Gly, Glu, Pro, Lys, 15 Ser, Met, or; Xaa at position 40 is Arg Asp Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu; Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly; Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, the Leu, Val or Lys; 20 Xaa at position 43 is\Asn/or Gly; Xaa at position 44 is Leu, Ger, Asp, Arg, Gln, Val, or Cys; Xaa at position 45 is Glu Tyr, His, Leu, Pro, or Arg; 25 Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr; Xaa at position 47 is Phe, Asn, Glu, Pro Lys, Arg, or Ser; Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile; 30 Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, Ris, Pro, Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys; Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, ox Ser; 35 Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;

```
Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
           Pro, or His;
     Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr,
           or His;
 5
     Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp,
            Gly, or Leu;
     Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;
     Xaa at poaition 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr,
           Gln, Trp, or Asn;
     Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg,
10
           or Asp;
     Xaa at position 39 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,
           or Arg;
     Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
15
     Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,
           Ser, Gln, or Leu;
     Xaa at position 62 is Ser Val, Ala, Asn, Trp, Glu, Pro,
           Gly, or Asp;
     Xaa at position 63 is Ile, Sex Arg, Thr, or Leu;
20
     Xaa at position 64 is Leu, Ala,
                                     Ser, Glu, Phe, Gly, or
     Xaa at position 65 is Lys, Thr, Gly Asn, Met, Arg, Ile,
           or Asp;
     Xaa at position 66 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
25
           or Arg;
     Xaa at position 67 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
           or Lys;
     Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
           Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
30
     Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;
     Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;
     Xaa at position 71 is Leu, Asn, Val, or Gln;
     Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;
     Xaa at position 73 is Leu, Ser, Trp, or Gly;
35
     Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;
     Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His,
```

25

30

Asn, or Ser;

- Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
 or Met;
- Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His;
- Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala, Oly, Ile or Leu;
- Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;
- 10 Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, His, Ala or Pro;
 - Xaa at position 8 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;
 - Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 15 Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;
 - Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr, Glu, Gln, Ser, Phe, Met, Val Lys, Arg, Tyr or Pro;
 - Xaa at position 85 is Ile, Leu Arg, Asp, Val, Pro, Gln, Gly, Ser, Phe, or His;
- 20 Xaa at position 86 is Lys, Tyr/ Leu, His, Arg, Ile, Ser, Gln, Pro;
 - Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val, Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;
 - Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or
 - Xaa at position 89 is Asp, or Ser;
 - Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala, Phe, or Gly;
 - Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Oln,
 Tyr, Leu, Lys, Ile, Asp, or His;
 - Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;
 - Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, Ser, Ala, or Pro;
- 35 Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;

20

Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg,
His, Glu, Ser, Ala or Trp;

Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;

Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;

Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile, Val or Asn;

Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or Leu

- 10 Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met;
 - Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Txp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile;
- 15 Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;
 - Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr;
 - Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg;
 - Xaa at position 106 is Asm, Ala Rro, Leu, His, Val, or Gln;
 - Xaa at position 107 is Ala, Ser, Tle, Asn, Pro, Lys, Asp, or Gly;
- 25 Xaa at position 108 is Gln, Ser, Met, Trp Arg, Phe, Pro, His, Ile, Tyr, or Cys;
 - Xaa at position 109 is Ala, Met, Glu, His, Sex, Pro, Tyr, or Leu;
- and which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding native amino acids of (1-133) human interleukin-3; and
- A pharmaceutically effective amount of a colony stimulating factor.

| 1 | | | | | | | | | | | | | | | |
|---|--|---|-------|-----|------|------|----------------|------------|----------|------|------|------|-----|-----|-----|
| | 19. The method of claim 18, wherein said human | | | | | | | | | | | | | | |
| \setminus interleukin-3 mutant polypeptide is of the Formula: | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | |
| 5 | neA | Cys | Xaa | Xaa | Xaa | Ile | Xaa | Glu | Xaa | Xaa | Xaa | Xaa | Leu | Lys | Xaa |
| | 1 | | | | 5 | | | | | 10 | | | | | 15 |
| | | | | | | | | | | | | | | | |
| | Xaa | Xaa | \Xaa | Xaa | Xaa | Xaa | Asp | Xaa | Xaa | Asn | Leu | Asn | Xaa | Glu | Xaa |
| | | | | | 20 | | | | | 25 | | | | | 30 |
| 10 | | | | | | | | | | | | | | | |
| | Xaa | Xaa | Ile | Leu | Met | Xaa | Xaa | Asn | Leu | Xaa | Xaa | Xaa | Asn | Leu | Glu |
| | | | | | 35 | | | | | 40 | | | | | 45 |
| | | | | | | | | | | | | | | | |
| | Xaa | Phe | Xaa | Xaa | Xaa | \Xaa | Xaa | Xaa | Xaa | Xaa | Asn | Xaa | Xaa | Xaa | Ile |
| 15 | | | | | 50 | | | | | 55 | | | | | 60 |
| | | | | | | | | | | | | | | | |
| | Glu | Xaa | Xaa | Leu | Xaa | Xaa | Leu | Xaa | Xaa | Cys | Xaa | Pro | Xaa | Xaa | Thr |
| | | | | | 65 | | | | | 70 | | | | | 75 |
| | | | | | | | | \searrow | | ^ | | | | | |
| 20 | Ala | Xaa | Pro | Xaa | Arg | Xaa | Xaa | *aa | ¥a# | Xaa | Xaa | Xaa | Gly | Asp | Xaa |
| | | | | | 80 | | | 1 | X | 85 | | | | | 90 |
| | | | | | | | | | / \ | 1 | | | | | |
| | Xaa | Xaa | Phe | Xaa | Xaa | Lys | Leu | Xaa | / Phe | Xa | Xaa | Xaa | Xaa | Leu | Glu |
| | | | | | 95 | - | | | | 100 | \ | | | | 105 |
| 25 | | | | | | | | | | | " | | | | |
| | Xaa | Xaa | Xaa | Xaa | Gln | Gln | [SEQ | DID | NO : 5 | 51 | / | | | | |
| | | | | | 110 | | , ~ ~ x | | | | | | | | |
| | | | | | | | | | | | | | | | |
| | wher | rein | | | | | | | | | | | | | |
| 30 | | | nosit | ion | 3 is | Ser | c, Gl | v. 2 | sn. | Met. | or | Gln: | | | |
| | | | | | | | 1, 01 1, Hi | | | | | , | | | |
| | | | | | | | | | | , | | | | | |
| | | Xaa at position 5 is Met or Ile; Xaa at position 7 is Asp or Glu; | | | | | | | | | | | | | |
| | | aa at position 9 is Ile, Ala, Leu, or Gly; | | | | | | | | | | | | | |
| 35 | | | | | | | le, V | | | | -11 | | | | / |
| | | _ | | | | | nr, H | | | | Ala: | | | | |

```
Xaa at position 12 is His or Ala;
     Xaa at position 15 is Gln, Asn, or Val;
     Xaa at position 16 is Pro, Gly, or Gln;
     Xaa at position 17 is Pro, Asp, Gly, or Gln;
 5
     Xàa at position 18 is Leu, Arg, Gln, Asn, Gly, Ala, or
           Glu;
     Xaa at position 19 is Pro or Glu;
     Xaa at Rosition 20 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
           Gln Glu, Ile, Phe, Thr or Met;
10
     Xaa at position 21 is Leu, Ala, Asn, Pro, Gln, or Val;
     Xaa at position 23 is Phe, Ser, Pro, or Trp;
     Xaa at position 24 is Asn or Ala;
     Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
           Leu, Met Tyr or Arg;
15
     Xaa at position 30 is Asp or Glu;
     Xaa at position 31 is An, Val, Met, Leu, Thr, Ala, Asn,
           Glu, Ser or Lys;
     Xaa at position 32 is Asp, Phe, Sex, Thr, Ala, Asn, Gln,
           Glu, His, Ile, Lys, Tyt, Val or Cys;
20
     Xaa at position 36 is Glu, Ala, Asn, Ser or Asp;
     Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or
           His;
     Xaa at position 40 is Arg or Ala;
     Xaa at position 41 is Arg, Thr, Val, Leu, or Gly;
     Xaa at position 42 is Pro, Gly, Ser, Gln Ala, Arg, Asn,
25
           Glu, Leu, Thr, Val or Lys;
     Xaa at position 46 is Ala or Ser;
     Xaa at position 48 is Asn, Pro, Thr, or Ile;
     Xaa at position 49 is Arg or Lys;
30
     Xaa at position 50 is Ala or Asn;
     Xaa at position 51 is Val or Thr;
     Xaa at position 52 is Lys or Arg;
     Xaa at position 53 is Ser, Phe, or His;
     Xaa at position 54 is Leu, Ile, Phe, or His;
35
     Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, or
           Gly;
```

```
Xaa at position 57 is Ala, Pro, or Arg;
     Xaa at position 58 is Ser, Glu, Arg, or Asp;
     Xaa at position 59 is Ala or Leu;
     Xaa at position 62 is Ser, Val, Ala, Asn, Glu, Pro, or
           Gly;
 5
     Xaa at position 63 is Ile or Leu;
     Xaa at Rosition 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
           G1\sqrt{\lambda}
               or Asp;
     Xaa at postion 66 is Asn, Gly, Glu, or Arg;
10
     Xaa at positton 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
           Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
     Xaa at position 69 is Pro or Thr;
     Xaa at position A is Leu or Val;
     Xaa at position 73\is Leu or Ser;
15
     Xaa at position 74 is Ala or Trp;
     Xaa at position 77 is Ala or Pro;
     Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or
           Arg;
     Xaa at position 81 is His,
                                 Pro, Arg, Val, Leu, Gly, Asn,
20
           Phe, Ser or Thr;
     Xaa at position 82 is Pro on Tyr;
     Xaa at position 83 is Ile or Wal
     Xaa at position 84 is His, Ile, Ask, Leu, Ala, Thr, Leu,
           Arg, Gln, Leu, Lys, Met, Ser, Yyr, Val or Pro;
25
     Xaa at position 85 is Ile, Leu, or Valy
     Xaa at position 86 is Lys, Arg, Ile, Gl\(\hat{\chi}\), Pro, or Ser;
     Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Asn,
           Ile, Leu or Tyr;
     Xaa at position 90 is Trp or Leu;
30
     Xaa at position 91 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
           Leu, Lys, Ile, Asp, or His;
     Xaa at position 92 is Glu, or Gly;
     Xaa at position 94 is Arg, Ala, or Ser;
     Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
35
     Xaa at position 98 is Thr, Val, or Gln;
     Xaa at position 100 is Tyr or Trp;
```

Xaa at position 101 is Leu or Ala; Xaa at position 102 is Lys, Thr, Val, Trp, Ser, Ala, His, Met, Phe, Tyr or Ile; Xaa at position 103 is Thr or Ser; 5 Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln; Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ale, Tyr, or Cys; Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr, 10 or Leu; which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 35 of the 15 amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3. 20. The method of claim 19, wherein said human interleukin-3 mutant polypeptide is of the Formula: 20 Asn Cys Xaa Xaa Met Ile Asp Gly xaa Ile Xaa Xaa Leu Lys Xaa 15 Xaa Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Deu Asn Xaa Glu Asp 25 20 25 30 Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu 35 40 45 30 Ala Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile 50 55 60

Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr 65 70 75

Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Gly Asp Trp

80 85 90 Xaa Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu 95 100 105 5 Xaa Xaa Xaa Gln Gln [SEQ ID NO:6] 110 wherein Xaa at position 3 is Ser, Gly, Asp, or Gln; 10 Xaa at position 4 is Asn, His, or Ile; Xaa at position & is Ile, Ala, Leu, or Gly; Xaa at position 11\is Thr, His, or Gln; Xaa at position 12 is His or Ala; Xaa at position 15 is An or Asn; Xaa at position 16 is Pro or Gly; 15 Xaa at position 18 is Leu, Arg, Asn, or Ala; Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr or Met; Xaa at position 21 is Leu Ma, Asn, or Pro; 20 Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu, Met, Tyr or Arg; Xaa at position 31 is Gln, Val, Met, Let, Ala, Asn, Glu or Lys; 25 Xaa at position 32 is Asp, Phe, Ser, Ala, Glu, Glu, His, Val or Thr; Xaa at position 36 is Glu, Asn, Ser or Asp; Xaa at position 37 is Asn, Arg, Pro, Thr, or His; Xaa at position 41 is Arg, Leu, or Gly; 30 Xaa at position 42 is Pro, Gly, Ser, Ala, Asn, Val, Let or Xaa at position 48 is Asn, Pro, or Thr; Xaa at position 50 is Ala or Asn; Xaa at position 51 is Val or Thr; 35 Xaa at position 53 is Ser or Phe;

Xaa at position 54 is Leu or Phe;

```
Xaa at position 55 is Gln, Ala, Glu, or Arg;
     Xaa at position 62 is Ser, Val, Asn, Pro, or Gly;
     Xaa at position 63 is Ile or Leu;
     Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly;
     Xaa at position 66 is Asn, Gly, Glu, or Arg;
 5
     Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
           His, Met, Phe, Ser, Thr, Tyr or Val;
     Xaa at position 73 is Leu or Ser;
     Xaa at position 74 is Ala or Trp;
10
     Xaa at position 77 is Ala or Pro;
     Xaa at position 79 is Thr, Asp, or Ala;
     Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser or
           Thr;
     Xaa at position 84 is His, Ile, Asn, Ala, Thr, Arg, Gln,
15
           Glu, Lys, Met, Ser, Tyr, Val or Leu;
     Xaa at position 85\is Ile or Leu;
     Xaa at position 86 As Lys or Arg;
     Xaa at position 8 / is Asp, Pro, Met, Lys, His, Pro, Asn,
           Ile, Leu of Tyr;
20
     Xaa at position 1 is Asn Pro, Ser, Ile or Asp;
     Xaa at position \4 i \sharpsi Arg, \Ala, or Ser;
     Xaa at position 95 is Ang, Thr, Glu, Leu, or Ser;
     Xaa at position 98 is Thi or Gin;
     Xaa at position 102 is Lys Val, Trp, or Ile;
25
     Xaa at position 103 is Thr, Ala, Ais, Phe, Tyr or Ser;
     Xaa at position 106 is Asn, Pro, Led, His, Val, or Gln;
     Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp;
     Xaa at position 108 is Gln, Met, Trp, Pae, Pro, His, Ile,
           or Tyr;
30
     Xaa at position 109 is Ala, Met, Glu, Ser, or Leu;
     and which can additionally have Met- or Met-Alat preceding
     the amino acid in position 1; and wherein from 4 to 26 of
     the amino acids designated by Xaa are different from the
35
     corresponding amino acids of native (1-133) human
     interleukin-3.
```

```
21.
                  The method of claim 20, wherein said human
     interleukin-3 mutant polypeptide is of the Formula:
 5
     Xaa at position 17 is Ser, Lys, Asp, Met, Gln, or Arg;
     Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
           Gln;
     Xaa at position 19 is Met, Arg, Gly, Ala, or Cys;
     Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
10
           Ala;
     Xaa at positian 21 is Asp, Phe, Lys, Arg, Ala, Gly, or
           Val;
     Xaa at position 20 is Glu, Trp, Pro, Ser, Ala, His, or
           Gly;
     Xaa at position 23 is Ile, Ala, Gly, Trp, Lys, Leu, Ser,
15
           or Arg;
     Xaa at position 24 is Il_e, Gly, Arg, or Ser;
     Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
           Ala;
20
     Xaa at position 26 is His, This, Phe, Gly, Ala, or Trp;
     Xaa at position 27 is Leu, $\frac{1}{2}$, Arg, Thr, Ser, or Ala;
     Xaa at position 28 is Lys/Leu, An, Gly, Pro, Val or Trp;
     Xaa at position 29 is Gln, Asn\ Pr\dot\, Arg, or Val;
     Xaa at position 30 is Pro, His, Thr,
                                           Gly, Asp, Gln, Ser,
25
           Leu, or Lys;
     Xaa at position 31 is Pro, Asp, Gly, Arg Leu, or Gln;
     Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or
           Glu:
     Xaa at position 33 is Pro, Leu, Gln, Thr, or Glu;
30
     Xaa at position 34 is Leu, Gly, Ser, or Lys;
     Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, or Cln;
     Xaa at position 36 is Asp, Leu, or Val;
     Xaa at position 37 is Phe, Ser, or Pro;
     Xaa at position 38 is Asn, or Ala;
35
     Xaa at position 40 is Leu, Trp, or Arg;
     Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, Pro;
```

```
Xaa at position 42 is Gly, Asp, Ser, Cys, or Ala;
     Xaa at position 42 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
           Cys, or Ser;
     Xaa\at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
 5
           Trp, or Pro;
     Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
           Lys or Trp;
     Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, or Gly;
     Xaa at position 47 is Ile, Gly, Ser, Arg, Pro, or His;
10
     Xaa at position 48 is Leu, Ser, Cys, Arg, His, Phe, or
           Asn;
     Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
           or Asp;
     Xaa at position 50 is Glu, Leu, Thr, Asp, or Tyr;
15
     Xaa at position 51 is Aşn, Arg, Met, Pro, Ser, Thr, or
           His;
     Xaa at position 52 is Asn,
                                 His, Arg, Leu, Gly, Ser, or
           Thr:
     Xaa at position 53 is Leu, Thr
                                     Ala, Gly, Glu, Pro, Lys,
20
           Ser, or;
     Xaa at position 54 is Arg, Asp Ile, Ser, Val, Thr, Gln,
           or Leu;
     Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
     Xaa at position 56 is Pro, Gly, Cys, Sex, Gln, or Lys;
25
     Xaa at position 57 is Asn or Gly;
     Xaa at position 58 is Leu, Ser, Asp, Arg, Cln, Val, or
           Cys;
     Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
     Xaa at position 60 is Ala, Ser, Tyr, Asn, or Thr;
30
     Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or
     Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, or 11e;
     Xaa at position 63 is Arg, Tyr, Trp, Ser, Pro, or Val;
     Xaa at position 64 is Ala, Asn, Ser, or Lys;
35
     Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or
           Ser;
```

10

15

20

25

30

35

```
Xaa at position 66 is Lys, Ile, Val, Asn, Glu, or Ser;
Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
      Pro, or His;
Xaa at position 68 is Leu, Val, Trp, Ser, Thr, or His;
Xaa at position 69 is Gln, Ala, Pro, Thr, Arg, Trp, Gly,
      or Leu;
Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
Xaa at position 71 is Ala, Met, Leu, Arg, Glu, Thr, Gln,
      Trp, or Asn;
Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg,
      or Asp;
Xaa at position \aleph is Ala, Glu, Asp, Leu, Ser, Gly, Thr,
      or Arg;
Xaa at position 74 is Ile, Thr, Pro, Arg, Gly, Ala;
Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,
      Ser, or Leu;
Xaa at position 76 is Ser Val, Ala, Asn, Trp, Glu, Pro,
      Gly, or Asp;
Xaa at position 77 is The, Ser, Arg, or Thr;
Xaa at position 78 is Led, Ala Ser, Glu, Gly, or Arg;
Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Ile, or
      Asp;
Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, or
      Arg;
Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, or
Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, or Asp;
Xaa at position 83 is Pro, Thr, Trp, Arg, ok Met;
Xaa at position 84 is Cys, Glu, Gly, Arg, Met or Val;
Xaa at position 85 is Leu, Asn, or Gln;
Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
Xaa at position 87 is Leu, Ser, Trp, or Gly;
Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His
      or Asn;
Xaa at position 90 is Ala, Ser, Asp, Ile, or Met;
```

Xaa at position 91 is Ala, Ser, Thr, Phe, Leu, Asp, or His;

Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, or Leu;

5 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;

Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, or Pro;

Xaa at position 95 is His, Gln, Pro, Val, Leu, Thr or Tyr;

10 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

Xaa at position 97 is Ile, Lys, Ala, or Asn;

Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, or Pro;

Xaa at position 99 is Ile, Arg, Asp, Pro, Gln, Gly, Phe, or His;

Xaa at position 100 is Lys, Tyr, Leu, His, Ile, Ser, Gln, or Pro;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, or Gln;

20 Xaa at position 102 is Gly Leu, Glu, Lys, Ser, Tyr, or Pro:

Xaa at position 103 is Asp, or Ser;

Xaa at position 104 is Trp, Val Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala, Phe, or Gly;

25 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, Leu, Lys, Ile, or His;

Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;

Xaa at position 108 is Arg, Asp, Leu, Thr, le, or Pro;

30 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyx, Leu, Ser, or Gly.

The method of claim 19 wherein said human interleukin-3 mutant polypeptide is of the Formula: 10 $(\text{Met})_m$ -Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr 5 15 20 Ser Trp Val Asn Cys Ser Xaa Xaa Xaa Asp Glu Ile Ile 25 30 35 Xaa His Leu\Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa 10 40 Xaa Asn Leu Ash Xaa Glu Asp Xaa Asp Ile Leu Xaa Glu 60 Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa 65 70 15 Ala Xaa Lys Xaa Leu Xaa, Asn Ala Ser Xaa Ile Glu Xaa 85 80 Pro Cys Xaa Pro Xaa Xaa Thr Ile Leu Xaa Asn Leu Xaa 90 100 Ala Xaa Pro Xaa Akg Xaa Pro Ile Xaa Ile Xaa Xaa Gly 20 105 115 Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu 125 120 Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln Thr Thr Leu 130 25 Ser Leu Ala Ile Phe [SEQ ID NO:7] wherein m is 0 or 1; Xaa at position 18 \(\) Asn or Ile; Xaa at position 19 is Met, Ala or Ile; Xaa at Rosition 20 is Ile, Pro or Ile; Xaa at position 23 is Ile, Ala or Leu; Xaa 30 at position 25 is Thr or His; Xaa at position 29 is Gln, Arg, Val or Ile; Xaa at position 32 is Leu, Ala,\Asn or Arg; Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe, Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at 35 position 45 is Gln, Val, or Met; Xaa at position 46 is Asp or Ser; Xaa at position 49 is Met, Ile, Leu or Asp; Xaa at

281

position 50 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at position 55 is Arg, Leu, or Thr; Xaa at position 56 is Pro or Ser; Xaa at position 59 is Glu or L'eu; Xaa at position 60 is Ala or Ser; Xaa at position 62 5 is\Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, \His or Gln; Xaa at position 69 is Gln or Glu; Xaa at position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at position 79 is Lys, Arg or Ser; Xaa at position 8% is Leu, Glu, Val or Trp; Xaa at position 85 is 10 Leu or Val; Xaa at position 87 is Leu, Ser, Tyr; Xaa at position 88 is Ala or Trp; Xaa at position 91 is Ala or Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or Thr; Xaa at position 98 is His, Ile, or Thr; Xaa 15 at position 100 is\Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at hosition 105 is Asn or Glu; Xaa at position 109 is Arg/, \dag{\pmu}u or Leu; Xaa at position 112 is Thr or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; Xaa at position 117 is Thr dr Ser; Xaa at position 120 is Asn, 20 Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3.

23. The method of claim 21 wherein said human interleukin-3 mutant polypeptide is of the Formula:

30 15 20

Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa 25 30 35

Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa Ile Leu Xaa Glu

282

40 45

Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa 50 55 60

Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa 65 70 75

Ile Leu Xaa Asn Xaa Xaa Pro Cys Xaa Pro Xaa Ala Thr

Ala Xaa kro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly 90 95 100

10 Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu 105 110

Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln [SEQ ID NO:8]

wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at 15 position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile: Xaa at position à is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xàa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Ile; Xaa at position 18 is Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; 20 Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at bosittion 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile or Asp; Xaa at position 36 is Glu or\Asp; Xaa at position 25 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala ox Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is Val or Ser; Xaa at position 30 53 is Ser, Asn, His or Gln; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or Trp; Xaa at position 71 is Leu or Val; 35 Xaa at position 73 is Leu, Ser or Tyr; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at

position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87 is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95 is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His; Xaa at position 109 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125) human interleukin-3.

24. The method of claim 22 wherein said human interleukin-3 mutant polypeptide is of the Formula:

15

20

10

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg Ais Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:9];

25

30

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:10];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leb 35 Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn

284

Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser

Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:11];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
10 Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
15 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:12];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Deu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:13];

25

30

35

20

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:14];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly

285

Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Tro Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:15];

Asn dys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
10 Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
15 Leu Glu Asn Ala Gln Ala Gln Gln (SEQ ID NO:16);

Asn Cys Ser Asn Mer Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Rro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:17];

25

20

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser

30 Ala

Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Cly Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:18];

35

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu

Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Qln Ala Gln Glu Gln Gln [SEQ ID NO:19];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu

10 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly

15 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:20];

Asn Cys Ser Asn Met the Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Deu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ IQ NO:21];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:22];

35

20

25

30

30

35

287

Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Olu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:23];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

10 Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly

15 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:24];

Met Ala Asn Cys Ser Asn Met Île Asp Glu Île Île Thr His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly

Glu Asp Gln Asp Île Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Île Glu Ala Île Leu Arg Asa Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Île Île Île Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr

Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:25];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Île Ile Thr His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Neu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:26];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu

35

288

Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Clu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:27];

Met Ala Ash Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly

Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:28];

Met Ala Asn Cys Ser Ile Met Île Asp Glu Île Île His His Leu
Lys Arg Pro Pro Asn Pro Yeu Leu Asp Pro Asn Asn Leu Asn Ser

20 Glu Asp Met Asp Île Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Île Glu Ser Île Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Île His Île Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr

25 Leu Glu Asn Ala Gln Ala Gln Gln [\$EQ ID NO:29];

Met Ala Asn Cys Ser Ile Met Ile Asp Clu Ile Ile His His Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:30];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35

289

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:31];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:32];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser

20 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr

25 Leu Glu Gln Ala Gln Glu Gln Gln [SEQ IQ NO:33];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

30 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:34];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

35

290

Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Tor Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:35];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro ro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:36];

Met Ala Asn Cys Ser Ile Net Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser

Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Aro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser

Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:37];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn

30 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:38];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

291

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Tro Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:39].

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Ser Asn Leu Glu Ser Pne Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Rhe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:40]

Met Ala Asn Cys Ser Ne Met Ile Asp Glu Ala Ile His His Leu

20 Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg Ris Pro Ile Ile Ile Lys Ala Gly

25 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:41]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp

Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Deu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ne Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr

Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:42]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala

292

Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Typ Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:43]

Met Ala Ash Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Rro Ala Pro Leu Leu Asp Pro Ash Ash Leu Ash Asp
Glu Asp Val Ser Ile Leu Met Glu Arg Ash Leu Arg Leu Pro Ash
Leu Glu Ser Phe Val Arg Ala Val Lys Ash Leu Glu Ash Ala Ser
Gly Ile Glu Ala Ile Leu Arg Ash Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:44]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:45]

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Deu Lys Arg Pro 30 Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Deu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:46]



Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:47] and

Met Ala Asn Cya Ser Ile Met Ile Asp Glu Leu Ile His His Leu
Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser

Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Clu Lys Leu Thr Phe Tyr Leu Val Thr

Leu Glu Gln Ala Gln Gln Gln Gln [SEQ ID NO:48].

- 25. The method of daim 23 wherein said human interleukin-3 mutant polypeptide is of the Formula:
- Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
 Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly
 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
 Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:32].
- 26. The method as recited in claim

 35 14,15,16,17,18,19,20,21,22,23,24 or 25 wherein said colony stimulating factor is selected from the group consisting of GM-CSF, G-CSF, and Meg-CSF.